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John Pafford

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EXAMINER

WALKER, AMANDA H

ART UNIT

PAPER NUMBER

3774

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

|                              |                                      |                                       |  |
|------------------------------|--------------------------------------|---------------------------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b><br>10/781,058 | <b>Applicant(s)</b><br>PAFFORD ET AL. |  |
|                              | <b>Examiner</b><br>AMANDA H. WALKER  | <b>Art Unit</b><br>3774               |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 15 October 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 2,3,73-75 and 77-116 is/are pending in the application.
- 4a) Of the above claim(s) 110-116 is/are withdrawn from consideration.
- 5) ☐ Claim(s) 83 and 84 is/are allowed.
- 6) ☐ Claim(s) \_\_\_\_\_ is/are rejected.
- 7) ☒ Claim(s) 83 and 84 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>10-15-07</u> .  | 6) <input type="checkbox"/> Other: _____                          |

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## **DETAILED ACTION**

### ***Status of the claims***

Claims 110-116 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Claims 1,4-72 and 76 have been cancelled. Claims 2,3,73-75,77-109 are pending for action.

### ***Response to Applicant's Arguments***

Applicant's arguments filed 10/15/07 have been fully considered and are persuasive.

### ***Priority***

Applicant has established a continuous priority chain for the claimed subject matter of "substantially pure osteogenic factor" and "impregnated" back to application SN 08/740031 filed on 10/23/1996 as stated in prior office actions.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 2, 3, 73, 77, 78, 80, 81, 90, and 93-100 are rejected under 35 U.S.C. 103(a) as being unpatentable over the University of Florida Tissue Bank, Inc. (as disclosed in applicant's own specification, para. 0012 in the PG-Pub) in view of Tucker et al. (United States Patent Number 5,674,292).

Regarding Claims 2, 3, 73, 77, 78, 80, 81, and 94-99, : Applicant discloses as prior art a diaphysial cortical dowel marketed by the University of Florida Tissue Bank, Inc. (hereafter UFTB) having the advantage of a naturally preformed cavity formed by the existing medullary canal of the donor long bone. The cavity can be packed with osteogenic materials such as bone or bioceramic (instant PG-Pub, para. 0012). This dowel is capable of being inserted between adjacent vertebrae, is inherently cylindrical, and is impregnated with an effective amount of a first osteogenic composition (either bone graft or bioceramic) which inevitably has osteogenic factors. It also inherently includes a wall capable of maintaining desired disc space height (instant PG-Pub, para. 0012). However, UFTB does not explicitly teach a substantially pure osteogenic factor.

Tucker et al. teach osteogenic devices containing a combination of osteogenic protein and a carrier/matrix (abstract). Tucker et al. go on to teach use of a large allogenic bone implant acting as a housing for the matrix/carrier containing the protein, which is to be placed in the cleaned marrow cavity (8:55-65). This protein may be a bone morphogenetic protein, whether recombinant or isolated from bone (3:20-30 and 6:1-22). It may be BMP 1, 2, 3, 4, 5, or 6, and may be a homo or heterodimer (4:50-60). Tucker et al. incorporates by reference United States Patent Number 5013649 (6:21), which teaches a method of producing purified (United States Patent Number 5013649, abstract) recombinant human BMP-2 (United States Patent Number 5013649, 6:40-46). The BMPs taught by Tucker et al. are assumed to be *substantially* pure due to the incorporation of United States Patent Number 5013649 (Tucker et al., 6:21), as well as the fact that no evidence to the contrary is present in the Tucker et al. document. Furthermore, the word “substantially pure” as broadly claimed encompasses an unknown range of potential impurities of which the Office has no means to define and therefore cannot patent over Tucker et al., which does not disclose *any* impurities. UFTB and Tucker et al. are combinable because

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they are from the same field of endeavor, namely, bone implants. At the time of the invention, it would have been obvious to a person having ordinary skill in the art to modify the osteogenic factor taught by UFTB with the proteins and matrix/carrier taught by Tucker et al., and one would have been motivated to do so since UFTB suggests impregnation with an osteogenic composition (instant PG-Pub, para. 0012) and Tucker et al. suggests use of its osteogenic compositions in a marrow cavity (8:55-65).

Regarding Claims 90 and 100-103 Tucker et al. teach that the first osteogenic factor is contained within a pharmaceutically acceptable carrier (see any example in 4:15-40). This may be polylactic acids, collagen, or calcium phosphates (4:15-25). In particular, Tucker et al. suggest use of one or more naturally derived molecules, for example, hydroxyapatite, tricalcium phosphate, collagen, and mixtures thereof (4:15-20). This could potentially include a situation where it was all tricalcium phosphate (i.e., a hydroxyapatite to tricalcium phosphate ratio of 0:100) (4:15-20).

Regarding Claim 93: A sponge is anything that is porous, and a strip or sheet is anything with one dimension that is longer than another. Tucker et al. teaches porous/sponge materials (3:40-50 and 3:60+) and UFTB teaches a dowel that implicitly a greater width than height or depth if inserted into the intervertebral space. This implies that it is a sheet or a strip.

Claims 73, 94, 85, and 104 are rejected under 35 U.S.C. 103(a) as being unpatentable over the Heggeness et al. (United States Patent Number 5,514,180) in view of Tucker et al. (United States Patent Number 5,674,292).

Heggeness et al. teach a cylindrical spinal spacer/dowel (figures, esp. FIGS. 24 and 25) impregnated with one or more osteogenic compositions containing one or more osteogenic factors (10:49+ and 11:25-40), or bone graft which inherently has osteogenic factors (10:43-46).

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The dowels have walls and are configured to be impacted into a concave space (FIGS. 24 and 25). However, Heggeness et al. does not explicitly teach a substantially pure osteogenic factor.

Tucker et al. teach osteogenic devices containing a combination of osteogenic protein and a carrier/matrix (abstract). Tucker et al. go on to teach use of a large allogenic bone implant acting as a housing for the matrix/carrier containing the protein, which is to be placed in the cleaned marrow cavity (8:55-65). This structure is analogous to FIG. 24 or Heggeness et al. Tucker et al. incorporates by reference United States Patent Number 5013649 (6:21), which teaches a method of producing purified (United States Patent Number 5013649, abstract) recombinant human BMP-2 (United States Patent Number 5013649, 6:40-46). The BMPs taught by Tucker et al. are assumed to be *substantially* pure due to the incorporation of United States Patent Number 5013649 (Tucker et al., 6:21), as well as the fact that no evidence to the contrary is present in the Tucker et al. document. Furthermore, the word “substantially pure” as broadly claimed encompasses an unknown range of potential impurities of which the Office has no means to define and therefore cannot patent over Tucker et al., which does not disclose *any* impurities. Heggeness et al. and Tucker et al. are combinable because they are from the same field of endeavor, namely, bone implants. At the time of the invention, it would have been obvious to a person having ordinary skill in the art to modify the osteogenic factor taught by Heggeness et al. with the purified proteins and matrix/carrier taught by Tucker et al., and one would have been motivated to do so since Heggeness et al. suggest impregnation with osteogenic compositions analogous to those taught in Tucker et al.

Regarding Claims 85 and 104: Heggeness et al. teach an embodiment having a tool engaging hole on the anterior wall (FIGS. 22 and 23). At the time of the invention, it would have been obvious to a person having ordinary skill in the art to combine the FIG. 25 embodiment with the FIG. 22/23 embodiment, and one would have been motivated to do so to gain the

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benefit of having the osteogenic composition cavities as well as the ability to manipulate the device with a tool.

Claims 74, 86-89, 105-109 are rejected under 35 U.S.C. 103(a) as being unpatentable over the Heggeness et al. (United States Patent Number 5,514,180) in view of Tucker et al. (United States Patent Number 5,674,292) as applied to claims 73, 85, 94, and 104 above, and further in view of Vich (United States Patent Number 4,877,020).

Regarding Claims 74, 86-89, 105 and 106: Heggeness et al. teach the basic bone dowel as applied to claims 73 and 94 above, as well as a hole for engaging an implanting tool as applied to claims 85 and 104 above. However, neither the outer surface of the bone dowel nor the hole for engaging an implanting tool is threaded.

Vich also teaches threaded cylindrical bone graft as well as a tool for inserting the bone graft. The bone graft has threads on both the outer surface (FIG. 1) as well as within the hole for engaging an implanting tool (FIGS. 1-3). The outer thread inherently creates teeth longitudinally along the surface of the dowel. These teeth inherently have crests between their leading and trailing flanks (FIG. 1). Furthermore, at some degree of magnification the outer thread will inherently have an area on its tooth crest that is flat. The bone dowel of Heggeness et al. and the bone dowel of Vich are combinable because they are from the same field of endeavor, namely, intervertebral spacing devices. At the time of the invention, it would have been obvious to a person having ordinary skill in the art to modify the device taught by Heggeness et al. with the threads as taught by Vich, and one would have been motivated to do so because threads are a well known mechanism by which to secure elements together, whether it be the outer surface of the dowel to bone or the inner surface of the dowel to the tool.

Regarding Claims 107-109: While Vich does not specifically teach the dimensions claimed, at the time of the invention, it would have been obvious to a person having ordinary skill in the art to optimize the threads to the specific height, width and angles claimed, and one would have been motivated to do so in order to adjust the entire implant size to fit the anatomy of a specific patient or to simply test for the optimal dimensions during routine experimentation (MPEP 2144.05 II).

Claim 82 is rejected under 35 U.S.C. 103(a) as being unpatentable over the University of Florida Tissue Bank, Inc. (as disclosed in applicant's own specification, para. 0012 in the PG-Pub) in view of Tucker et al. (United States Patent Number 5,674,292) as applied to claims 73 and 80 above, and further in view of Heggeness et al. (United States Patent Number 5,514,180).

UFTB teaches the basic spinal spacer impregnated with an effective amount of a first osteogenic composition and osteogenic factor. Tucker et al. teaches that the factor is substantially pure as well as use of a marrow cavity as a carrier for BMP. However, neither document teaches that there are multiple osteogenic factors.

Heggeness et al. teaches an intervertebral device (FIG. 24) having a body 71 and a chamber 73. The chamber is packed with at least one osteoinductive material (10:49-52). Preferably, the osteoinductive material(s) are incorporated in a matrix (10:49-52 and 11:25-40). The osteoinductive materials may be one or more of any of the claimed BMPs (10:48-60). UFTB and Heggeness et al. are combinable because they are from the same field of endeavor, namely, intervertebral spacers. At the time of the invention, it would have been obvious to a person having ordinary skill in the art to modify the osteogenic material packed into the marrow cavity as taught by UFTB and Tucker et al. with the multiple osteogenic materials as taught by



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Heggeness et al., and one would have been motivated to do so because common knowledge would lead one to believe that more osteogenic factors would cause more osteogenesis, which would in turn cause faster healing.

Claims 90 and 91 are rejected under 35 U.S.C. 103(a) as being unpatentable over the UFTB (United States Patent Number 5,514,180) in view of Tucker et al. (United States Patent Number 5,674,292) as applied to claim 73 above, and further in view of Kuberasampath et al. (United States Patent Number 6077988).

UFTB teaches the basic dowel filled with an osteogenic composition and inherent osteogenic factors as applied above. Tucker teaches purification of the osteogenic factors. However, neither reference teaches use of a carrier such as physiological saline.

Kuberasampath et al. teaches an osteogenic protein dispersed within a porous matrix to be implanted into the body (1:5-15). Kuberasampath et al. suggests use of the matrix instead of bone grafts for increased osteoinductivity (1:55-60). The matrix comprises a polymer of cross linked collagen and GAG and dispersed with an osteogenic protein. The osteogenic protein may be dispersed in a solvent such as buffered saline (3:45-65). UFTB and Kuberasampath et al. are combinable because they are from the same field of endeavor, namely, bone implants capable of being used in the intervertebral disc space. At the time of the invention, it would have been obvious to a person having ordinary skill in the art to modify the bone or bioceramic filling material taught by UFTB with the matrix dispersed with osteogenic protein taught by Kuberasampath et al., and one would have been motivated to do so because Kuberasampath et al. suggests that it will have increased osteoinductivity (1:55-60).

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Claims 90 and 92 are rejected under 35 U.S.C. 103(a) as being unpatentable over the UFTB (United States Patent Number 5,514,180) in view of Tucker et al. (United States Patent Number 5,674,292) as applied to claim 73 above, and further in view of Brekke (United States Patent Number 5,366,508).

UFTB teaches the basic dowel filled with an osteogenic composition and inherent osteogenic factors as applied above. Tucker teaches purification of the osteogenic factors. However, neither reference teaches use of a carrier buffered sterile water.

Brekke teaches a device that when implanted into a bone defect can restore mechanical integrity and initiate osteogenesis. This device has a porous macro and microstructure complex (8:49-60). Prior to implantation, the complex is injected with a solution containing BMPs (8:60+). This solution carrying the BMPs may be sterile water (8:64). UFTB and Brekke are combinable because they are from the same field of endeavor, namely, bone implantation materials suitable for delivery into the intervertebral space. At the time of the invention, it would have been obvious to a person having ordinary skill in the art to modify the osteogenic material taught by UFTB with the complex injected with sterile water carrying BMPs as taught by Brekke, and one would have been motivated to do so in order to take advantage of potential benefits gained by using a polylactate and hyaluronic acid porous complex to carry the osteogenic factors, such as decreased immune response.

The following prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

4961740: threaded dowel with dimensions

5593409: threaded dowel with dimensions

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***Allowable Subject Matter***

Claims 83 and 84 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

***Conclusion***

Applicant's arguments with respect to the claims have been considered but are moot in view of the new ground(s) of rejection.

***Correspondence***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AMANDA H. WALKER whose telephone number is (571)270-3296. The examiner can normally be reached on 8-5, M-Th, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Corrine McDermott can be reached on (571) 272-4754. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Alvin J Stewart/  
Primary Examiner, Art Unit 3774

AHW  
3-4-08